

Claims

1. A method for determining the conformational state of a protein, comprising the steps of:

a) contacting a protein with a first binding partner which is capable of binding to the protein in a manner dependent on the conformational state of the protein and which generates a signal in a manner dependent on the binding of the first binding partner to the protein; and

b) detecting labelling of said protein by the binding of the first binding partner to said protein, wherein labelling of said protein is an indicator of the conformational state of said protein.

2. A method for measuring the activity of an enzyme, wherein the conformation of a protein is dependent upon the post-translational modification activity of the enzyme, the method comprising the steps of:

a) contacting a protein comprising a site for post-translational modification with the enzyme;

b) providing a first binding partner which is capable of binding to the protein in a manner dependent on the post-translational modification of the protein by the enzyme and which generates a signal in a manner dependent on said post-translational modification; and

c) contacting the protein with the first binding partner and determining the post-translational modifying activity of the enzyme.

3. The method of claim 1 or claim 2, further comprising the steps of:

- (i) providing a second binding partner, capable of binding to the protein; and
- (ii) contacting the protein with the second binding partner.

4. The method of any one of claims 1 to 3, wherein the protein is immobilised on a solid phase substrate.

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5. The method of claim 3, wherein the second binding partner is a capture ligand, and the protein is isolated by binding to said capture ligand.

6. The method of claim 5, wherein said capture ligand is bound to a solid phase support.

7. The method of claim 1 or claim 2, wherein said first and/or second binding partner is labeled with a label selected from the group consisting of a fluorescent or other luminescent label, a domain of an enzyme, a radiolabel, a chemical or enzymatic label and a heavy metal or other radioopaque label.

8. The method of claim 1 or claim 2, wherein said first binding partner is labelled with a label detectable in a manner dependent on the binding of said first binding partner to the protein.

9. The method of claim 3, wherein said second binding partner is labelled.

10. The method of claim 9, wherein both said first and second binding partners are labelled, the labels are fluorescent and the binding of said binding partners to the protein is assayed by FRET.

11. The method of claim 8, wherein both said first and second binding partners are labelled, the labels are enzyme domains, which associate to form a functional reporter molecule when both binding partners are bound to the protein.

12. The method of claim 4, wherein said protein is covalently linked to the solid phase substrate.

13. The method of any one of claims 4 to 6 or 12, wherein unbound labelled

binding partner is removed to allow detection of the binding of the labelled binding partner to the protein.

14. The method of claim 8, wherein the labelling of the protein by the binding of said first binding partner is detected by FCS.

15. A first binding partner which binds to a protein, which binding partner:
a) binds to the protein in a manner dependent on the conformational state of the protein; and
b) is detectable in a manner dependent on its binding to the protein.

16. The first binding partner of claim 15, which is an antibody.

17. The first binding partner of claim 16, which is a single-chain antibody or scFv.

18. The first binding partner of claim 15, which is a peptide ligand.

19. A kit for the determination of the conformational state of a protein in a sample, comprising:
a) a first binding partner according to claim 15; and
b) packaging components.

20. A kit for the determination of the presence of a ligand for a protein in a sample, comprising:
a) a protein which binds to the ligand the presence of which is to be determined and which undergoes conformational change as a result of such binding;
b) a first binding partner according to claim 15 which binds to the protein in a conformationally-dependent manner; and
c) packaging components.

21. The kit of claim 19 or claim 20, which further comprises a second binding partner.

22. The kit of claim 21, wherein the first and/or the second binding partner is labelled.

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